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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/912,818	07/24/2001	Daniel Pinkel	407E-914026US	8113

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 05/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/912,818	PINKEL ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2005* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-70, 74-76* is/are pending in the application.

4a) Of the above claim(s) _ is/are withdrawn from consideration.

5)☒ Claim(s) *45-67* is/are allowed.

6)☒ Claim(s) *68-71 and 74-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status

1. Claims 45-70 and 74-76 are pending.

Claims 45-67 are allowed (in view of the terminal disclaimer).

Claims 68-70, 74-76 are rejected.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 68, 69, 74 and 75 are rejected under 35 U.S.C. 102(b) as being anticipated by Lavialle et al (Anticancer Research (1989) 9:1265-1280).

Lavialle teaches method for detecting a copy number variation in a suspected breast cancer sample (see page 1267, figure 1, page 1266, column 2 and page 1269, column 1, line 5)

on chromosome 17, from position q22 to position q24 (page 1269, column 1, lines 3-6, where Lavialle states "However, in this case, cells without DMs still have a high level of c-myc amplification (30 fold) and the c-myc copies are integrated into an ABR at 17q24.")

said method comprising:

(a) contacting a probe that binds selectively to a target polynucleotide sequence of said region with a nucleic acid sample prepared, directly or indirectly, from said suspected breast cancer sample, wherein said nucleic acid sample comprises said target polynucleotide sequence and said probe is contacted with said sample under conditions in which said probe fonns a stable hybridization complex with said target nucleic acid sequence (see page 1267, figure 1, where c-myc probes were hybridized to determine chromosomal location in SW-613 cells which are prepared indirectly from a breast cancer sample); and

(b) detecting said hybridization complex (see page 1267, figure 1).

With regard to claim 69, Lavialle teaches a labeled probe (see page 1267, figure 1, "hybridized to ^{3}H-labeled c-myc probe").

With regard to claim 74, Lavialle teaches hybridization in situ to whole cells, which inherently comprises genomic DNA (see page 1267, figure 1).

With regard to claim 75, Lavialle teaches detection of nucleic acids which were in cells propagated and therefore containing amplified amounts of the starting nucleic acid (see figure 4, for example).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 70 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lavialle et al (Anticancer Research (1989) 9:1265-1280) in view of Mullis et al (U.S. Patent 4,683,202).

Lavialle teaches method for detecting a copy number variation in a suspected breast cancer sample (see page 1267, figure 1, page 1266, column 2 and page 1269, column 1, line 5)

on chromosome 17, from position q22 to position q24 (page 1269, column 1, lines 3-6, where Lavialle states "However, in this case, cells without DMs still have a high level of c-myc amplification (30 fold) and the c-myc copies are integrated into an ABR at 17q24.")

said method comprising:

(a) contacting a probe that binds selectively to a target polynucleotide sequence of said region with a nucleic acid sample prepared, directly or indirectly, from said suspected breast cancer sample, wherein said nucleic acid sample comprises said

target polynucleotide sequence and said probe is contacted with said sample under conditions in which said probe fonns a stable hybridization complex with said target nucleic acid sequence (see page 1267, figure 1, where c-myc probes were hybridized to determine chromosomal location in SW-613 cells which are prepared indirectly from a breast cancer sample); and

(b) detecting said hybridization complex (see page 1267, figure 1).

With regard to claim 69, Lavialle teaches a labeled probe (see page 1267, figure 1, "hybridized to ^{3}H-labeled c-myc probe").

With regard to claim 74, Lavialle teaches hybridization in situ to whole cells, which inherently comprises genomic DNA (see page 1267, figure 1).

With regard to claim 75, Lavialle teaches detection of nucleic acids which were in cells propagated and therefore containing amplified amounts of the starting nucleic acid (see figure 4, for example).

Lavialle does not teach PCR amplification of the DNA to form a labelled sample before detection or the use of cDNA.

Mullis teaches a polymerase chain reaction amplification method in which DNA is amplified prior to detection (see column 13, line 42 to column 14, line 17). Mullis further teaches the use of any DNA source, including cDNA (see column 5, lines 35-60). Mullis further teaches labeling of the sample DNA (see column 14, lines 8-17).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to amplify the sample of Tsuda as taught by Mullis since Mullis states

> "The method herein may also be used to enable detection and/or characterization of specific nucleic acid sequences associated with infectious diseases, genetic disorders or cellular disorders such as cancer. Amplification is useful when the amount of nucleic acid available for analysis is very small, as, for example, in the prenatal diagnosis of sickle cell anemia using DNA obtained from fetal cells. Amplification is particularly useful if such an analysis is to be done on a small sample using non-radioactive detection techniques which may be inherently insensitive, or where radioactive techniques are being employed but where rapid detection is desirable. (see column 13, lines 42-54)."

Thus, Mullis provides explicit motivation to amplify cancer related genes, such as the genes identified by Tsuda as associated with breast cancer, in order to perform rapid detection, which will minimize possible anxiety for breast cancer patients subject to the test, as well as more sensitive detection, to ensure that the cancer is detected even when the amount of material is very small. The practitioner in 1992 would have expected the PCR method of Mullis to function with a near absolute expectation of success.

Response to Arguments

7. Applicant's arguments filed March 24, 2005 have been fully considered but they are not persuasive.

Applicant attempts to amend the claim by parsing a difference between the word "at" and the word "from". In particular, Applicant argues that the amplification of Lavialle may be "at" 17q22-24, but that the amplified c-myc sequences are "from" 8q24. This

argument is not persuasive for three different reasons. First, in the patient sample that Lavialle uses, the c-Myc sequences are "from" 17q22-24. While in a noncancerous sample from that patient, or in most samples from other individuals, c-myc is found only at 8q24, that does not disturb the fact that in the particular sample of Lavialle, the sequences at issue are "from" 17q22-24. Second, to the extent that the argument is centered on the origin of "unique sequences from 17q22-24", this argument represents an attempt to import a product by process type limitation into the method claim. Applicant appears to wish that the 17q22-24 region be limited to nucleic acids which are originally from 17q22-24, rather than ones like c-myc that are translocated to that region. However, to the extent that specific structure exists, none is implied by the claim. The use of the word "from" does not imply any particular structure for the 17q22-24 region and will not define the invention over the Lavialle reference. Third, the argument that sequences "normally present" at 17q22-24 are not detected by Lavialle demonstrates Applicant's intention to read limitations into the claims (which are likely not supported by the specification). The claim incorporates no requirement that the sequence being amplified is the sequence "normally present" at the particular region. This cannot be called an attempt to read the specification into the claims, however, since the specification does not describe any sequence which is normally present at 17q22-24.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
9/5/05